IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
Group Art Unit 1633

In re

Patent Application of

Ralph R. Weichselbaum, et al.

Application No. 08/289,290

Confirmation No.: 1375

Filed: August 11, 1994

Examiner: Li, Qian Janice

"CONSTITUTIVE GENE EXPRESSION IN CONJUNCTION WITH IONIZING RADIATION"

Signature

April 12, 2007
Date of Signature

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

REQUEST FOR REHEARING

APPEAL NO. 2006-0141

Mail Stop Appeal Brief- Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In reference to Appeal No. 2006-0141, and in response to the Decision on Appeal of the Board of Patent Appeals and Interferences dated February 12, 2007, Appellants request a rehearing by the Board of Patent Appeals and Interferences pursuant to 37 C.F.R. § 41.52. Specifically, Appellants request reconsideration by the Board of its decision affiming the Examiner's rejection of claims 29 and 37 under 35 USC § 103(a) as obvious over U.S. Patent No. 6,143,290 ("the Zhang reference") in view of Walther et al., Anticancer Research 13: 1565-1574 (1993) Retrovirus Mediated Gene Transfer of Tumor Necrosis Factor Alpha into Colon Carcinoma Cells Generates a Growth Inhibition ("the Walther reference").

APPELLANTS' ARGUMENT IN VIEW OF THE DECISION OF THE BOARD

In the present Request for Rehearing, and pursuant to 37 CFR § 41.52, Appellants herein discuss with particularity the points misapprehended and overlooked by the Board in its Decision dated February 12, 2007 ("the Decision").[1] Specifically, in the Decision, which affirmed the Examiner's rejection of claims 29 and 37 as obvious over the Zhang reference in view of the Walther reference,[2] the Board did not address Appellants' arguments regarding the Examiner's application of the test for obviousness.

Claim 29, which the Board selected as the representative claim to decide the appeal (Decision, page 2), is directed to a pharmaceutical composition comprising a genetic construct comprising a nucleic acid that encodes a TNF-α operatively linked to a constitutive promoter dispersed in a pharmacologically acceptable carrier, wherein the genetic construct is packaged within an adenovirus particle. Claim 37, the only other claim subject to the instant appeal, is directed to the composition of claim 29 wherein the adenovirus particle contains a deletion of the E1 region and/or the E3 region of the adenoviral genome.

A. The Board Did Not Properly Consider "Motivation to Combine"

The Board concluded that the references provided motivation to combine their disclosures, but failed to address Appellant's arguments made in the Reply Brief dated March 8, 2005.

The Board's conclusion appears to rest on Zhang et al.'s hypothesis that the adenoviral vectors disclosed therein could be used to deliver "other related genes for human cancer therapy," and Zhang et al.'s observation that "major problems are associated

[1] Familiarity with the Appeal Brief, Examiner's Answer, Reply Brief and Decision is presumed.

[2] Footnotes 3 and 4 of the Decision state that Appellants do not dispute Zhang et al.'s or Walther et al.'s qualifications to be prior art to the claims. However, nothing in the record indicates that Appellants have made any such concession. Indeed, Appellants reserve the right to antedate either or both of the Zhang and Walther references in future prosecution.

with using retroviral vectors for gene therapy." (Decision, FF2 and FF5, and pages 9-10). However, the mere mention of "other related genes," even coupled with Zhang et al.'s criticism of retroviral vectors, does not provide motivation to use an adenoviral vector with TNF-α, as in Appellants' claims. First, the Board appears to have misapprehended "other related genes" to include TNF-α. The Decision does not address Appellants' argument that TNF-α is not "related" to p53 and antisense oncogenes, which are "growth control-related" agents that act on tumors directly. (Reply Brief, page 5). Unlike p53 and antisense oncogenes, TNF-α exhibits anti-cancer effects by modulating the type and duration of the immune response against tumor cells. Nothing in the present record, or in the art generally, correlates TNF-α as "related" to p53. (Reply Brief, page 5). Second, the Board did not address Appellants' arguments that the Zhang reference, at most, suggests that retroviral vectors are problematic for the delivery of p53, or other growth control-related genes, to cells. (Reply Brief, page 5). The Zhang reference does not suggest to one of skill in the art that adenovirus should be used as a substitute for retrovirus for every conceivable therapeutic application of gene therapy using viral vectors. (Reply Brief, pages 5-6).

Similarly, Walther et al., while disclosing delivery of TNF-α to cells via a retroviral vector, make no mention or suggestion that such a retroviral vector would be, or should be, interchangeable with other types of vectors, including adenoviral vectors. Thus, neither reference provides any motivation to combine or modify Walther et al. and/or Zhang et al. to produce the pharmaceutical composition presently claimed in claims 29 and 37.

B. The Board Did Not Properly Consider "Reasonable Expectation of Success"

The "reasonable expectation of success" factor must be considered in determinations of obviousness. *Micro Chem., Inc. v. Great Plains Chem. Co.*, 103 F.3d 1538, 1547, 41 USPQ2d 1238, 1245 (Fed. Cir. 1997) ("The consistent criterion for determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out and would have a reasonable likelihood of

success, viewed in the light of the prior art.") While the Board recognized the appropriate obviousness standard in the Decision, the Board merely made conclusory statements that one of skill in the art would reasonably expect success, and did not address Appellants' arguments made in the Reply Brief.

The Board has not established a legally sufficient basis to support its conclusions that:

- "[o]ne of skill in the art, reading Zhang, would reasonably expect that an adenovirus construct could carry the gene expressing TNF-α and be applicable in human cancer therapy."
- "would reasonably expect an adenovirus construct for delivering the gene expressing TNF-α for human cancer therapy to be an improvement over a retroviral vector for doing the same (i.e., Walther)."
- "Zhang provides sufficient motivation to arrive at the claimed invention with a reasonable expectation of success given the disclosures of Zhang and Walther."

(Decision, pages 10-11).

Appellants asserted that that the choice of viral vector for any particular therapeutic application is dependent on a number of factors that affect the desired outcome, i.e., whether a vector will be successful in a given application. (Reply Brief, page 6). Appellants argued that one of skill in the art must consider:

- whether the polypeptide encoded by the vector construct is likely to interact with viral replication and/or packaging.
- whether viral products may interfere with trafficking or therapeutic function of the polypeptide delivered to the cell.
- whether the host immune response against the viral vector or encoded polypeptide will preclude therapeutic efficacy.

(Reply Brief, page 6).

Because the cited references do not provide any indication as to how to solve or circumvent these problems with respect to the claimed composition, there would have been no reasonable expectation of success here. See, e.g., *In re Vaeck*, 947 F.2d 488,

493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991) ("Both the suggestion and the reasonable expectation of success must be found in the prior art, not in the applicant's disclosure.")

C. CONCLUSION

In summary, Appellants argued in the Reply Brief that the Examiner did not properly apply the "motivation to combine" and "reasonable expectation of success" factors of the test for obviousness, and the Board did not address these arguments. When the present record is considered as a whole, it is clear that one of skill in the art would not have been motivated to mix and match the disclosures of Zhang et al. and Walther et al. to arrive at the claimed invention. Moreover, even assuming *arguendo* that motivation was present, the present record does not support the conclusion that one of skill in the art would have reasonably expected that substituting the retroviral vector of Walther et al. with the adenoviral vector of Zhang et al. in a construct encoding TNF-α would successfully produce the pharmaceutical composition of claims 29 and 37.

In view of the foregoing, Appellants respectfully request reconsideration by the Board of its Decision and further request reversal of the Examiner's rejection of claims 29 and 37 under 35 U.S.C. § 103.

Respectfully submitted,

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